Docket No. 0975.1005-056
Title: Methods of Treating Neurodegenerative........

Inventors: Junming Le, et al.

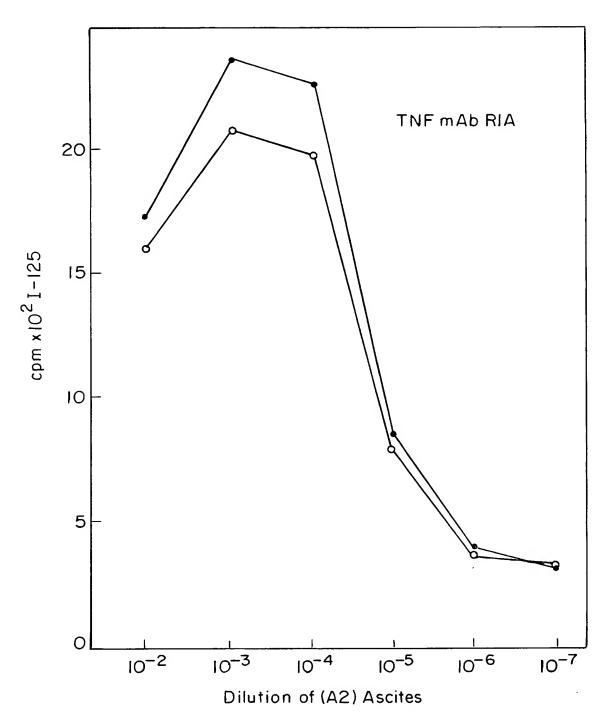


FIG. 1

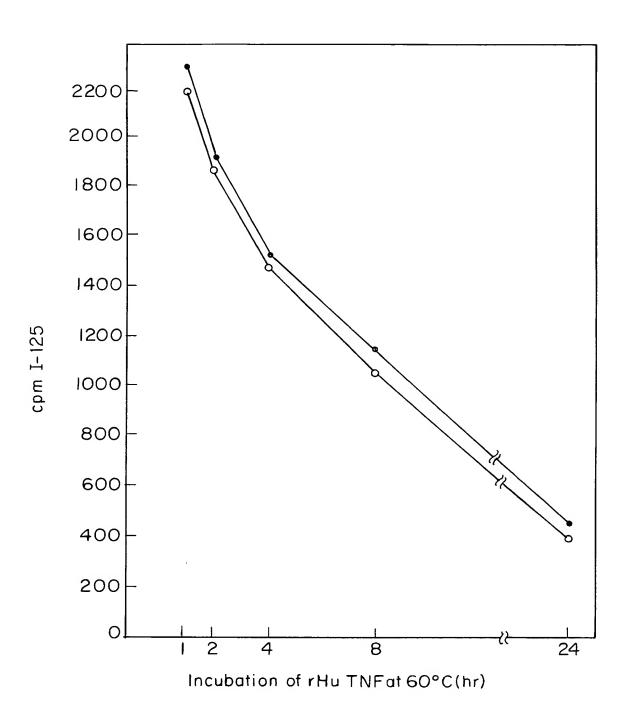
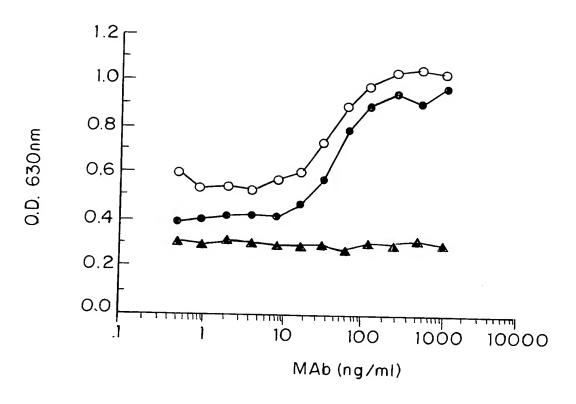


FIG. 2

Title: Methods of Treating Neurodegenerative........
Inventors: Junming Le, et al.

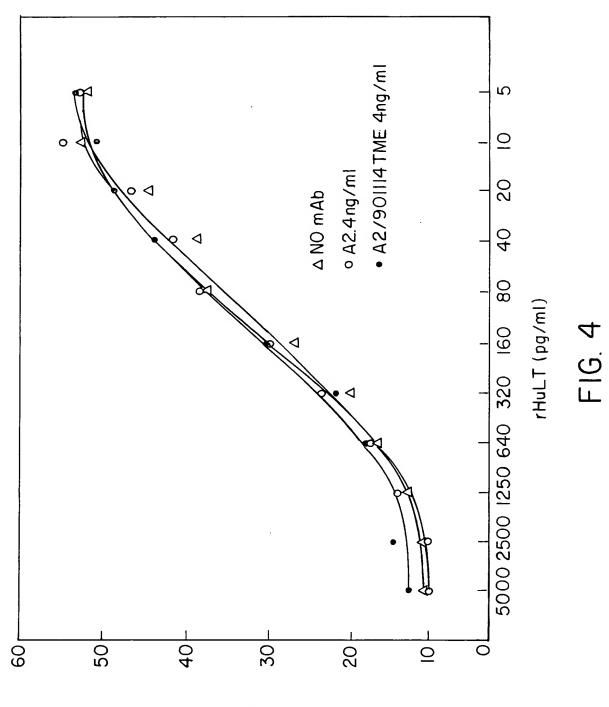


- Natural Human TNF
- Recombinant Human TNF
- ▲ Control

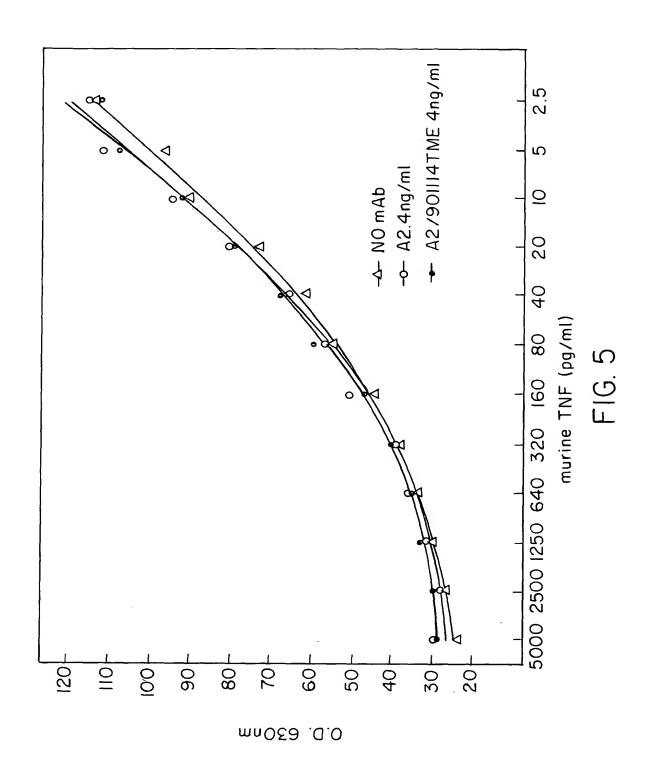
FIG. 3

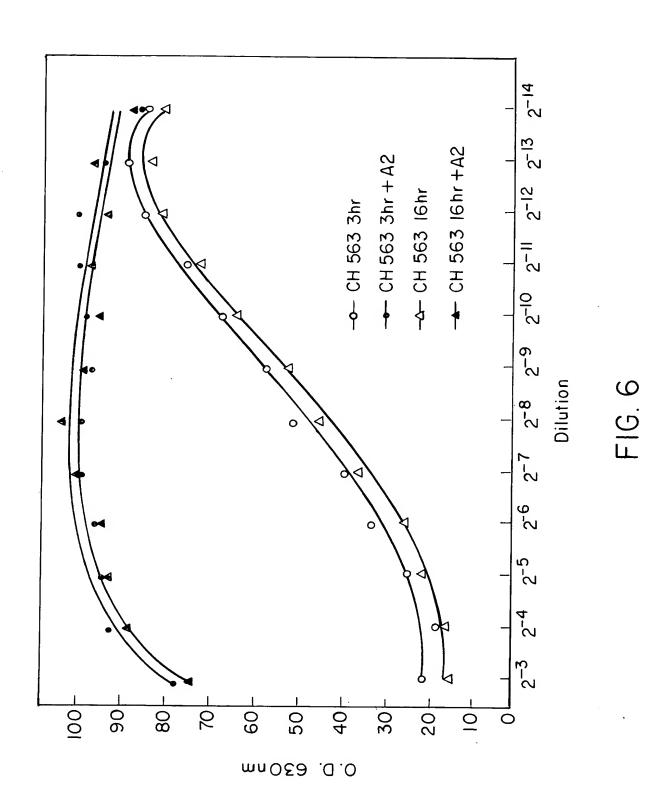
Docket No. 0975.1005-036

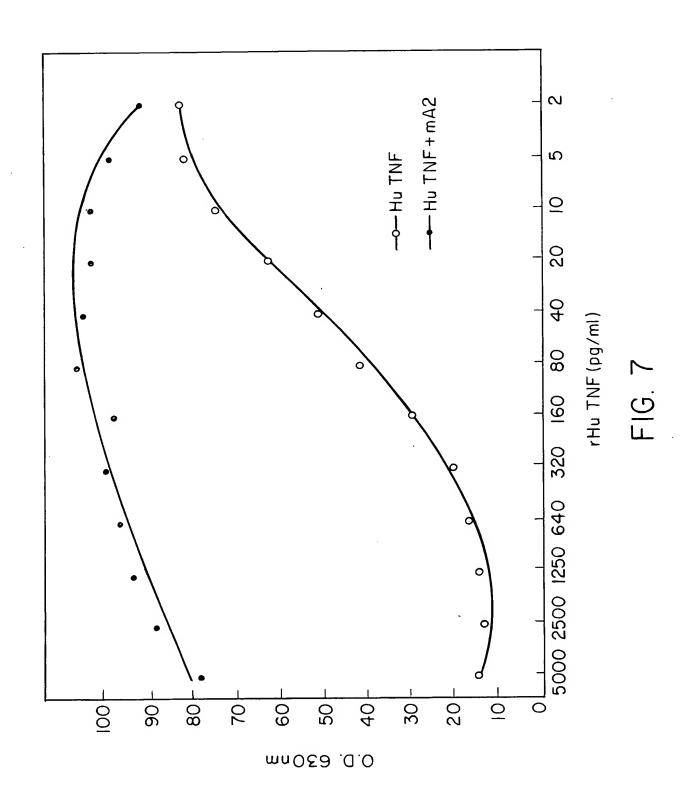
Title: Methods of Treating Neurodegenerative.......
Inventors: Junming Le, et al.



mn059 .0.0







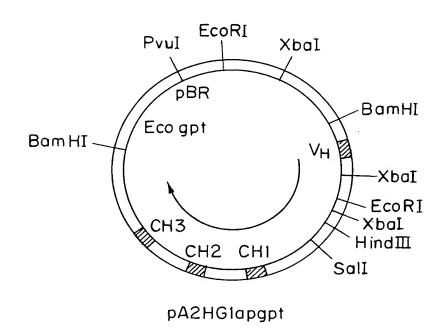


FIG. 8A

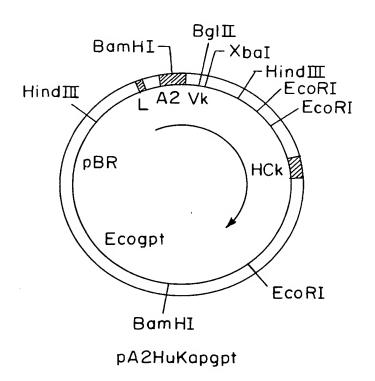


FIG. 8B

Title: Methods of Treating Neurodegenerative..........
Inventors: Junming Le, et al.

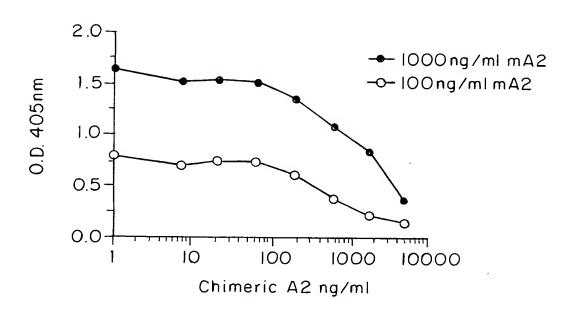


FIG. 9A

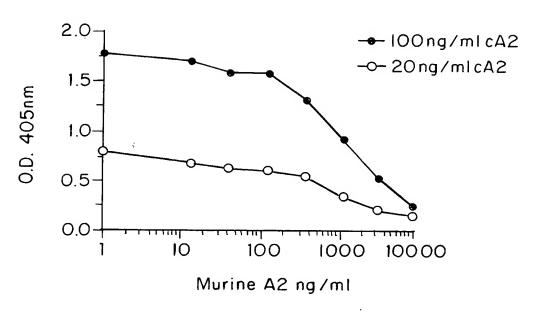
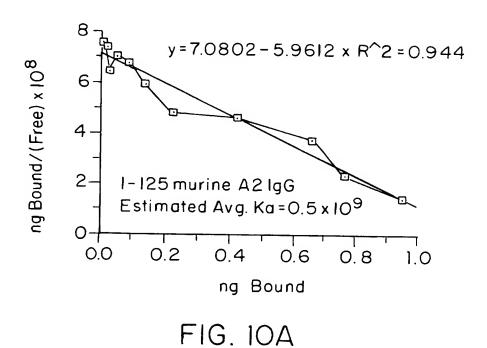
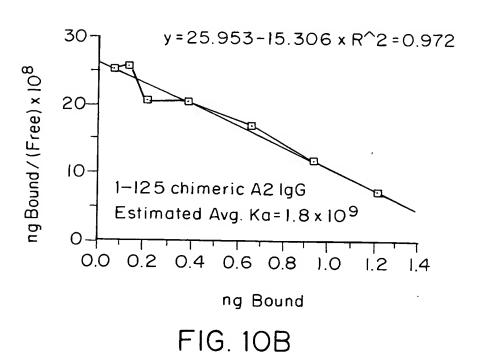


FIG. 9B





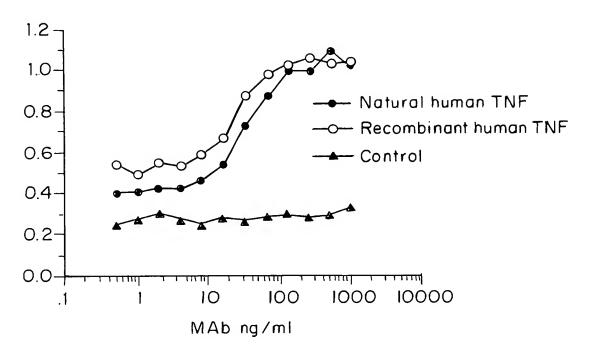


FIG. 11

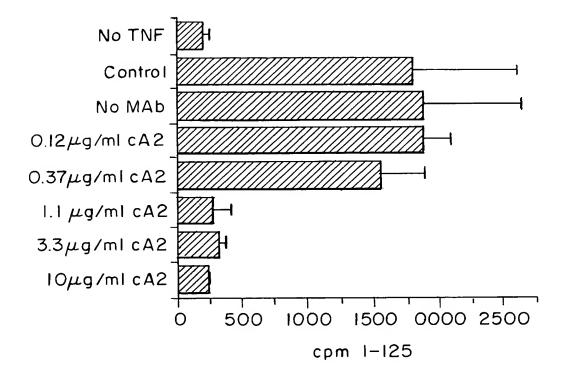


FIG. 12

Pro	Gly	Ser	Ile	Pro	Leu	Asp	
Asn	Asn	Tyr	\mathtt{Thr}	Ser	Tyr	Pro	
Ala	Ala		His	Lys	Ile	Arg	
Val	Leu Ala	Leu Ile	Thr	Ile	Pro	Ile Asn	Leu
		$T\gamma r$	Leu	Ala	Glu	Ile	Ala
His Val	Ala Leu	Leu	Leu	Ser	Tyr Glu	Glu	Ile
Ala		Ser Glu Gly Leu	Val	Leu	Trp	Leu Ser Ala Glu	Phe Gly Ile Ile Ala
Pro Val	Arg Ala Asn	Glu	His	Asn Leu	Lys Pro	Ser	Gly
Pro	Arg		Thr	Asn	Lys		Phe
Lys	Arg	Pro	Ser	Val	Ala	130 Asp Arg	150 Val Tyr
10 Asp	30 Asn	50 Val	70 Pro	90 Lys	110 Glu	130 Asp	150 Val
Pro Ser	Trp Leu	Val	Cys	Thr	Ala	Lys Gly	Gly Gln
		Leu	Gly Cys	Gln	${\tt Gl}{\tt y}$		${ t Gly}$
Arg Thr	Gln	Gln	Gly Gln	Tyr	Glu	Leu Glu	Ser
Arg	Leu	Asn	${\tt Gly}$	Ser	Pro	Leu	Glu
Ser	Gln	Asp	Lys	Val	\mathtt{Thr}	Phe Gln	Ala
Ser	Ala Glu Gly Gln	Glu Leu Arg	Phe	Ala	Glu	Phe	Leu Asp Phe Ala
Ser	Glu	Leu	ren	Ile	Gln Arg	Gly Val	Asp
Arg 8	Ala		Val	Arg		$\mathtt{G1}\mathtt{y}$	Leu
1 Val	21 Gln	41 Val	61 Gln	81 Ser	101 Cys	121 Gly	141 Tyr

FIG. 1

Docket No. 0975.1005-030 Title: Methods of Treating Neurodegenerative.......

Inventors: Junming Le, et al.

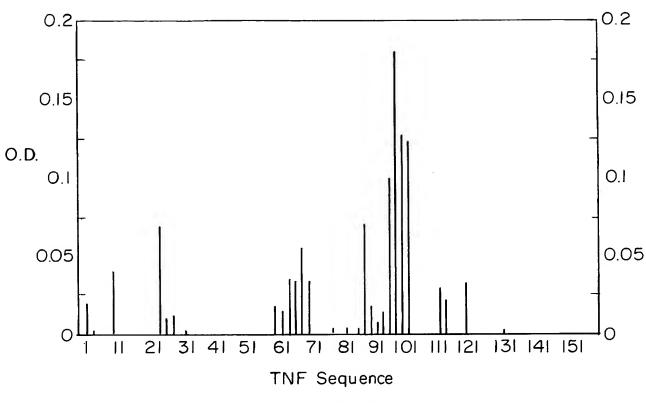


FIG. 14A

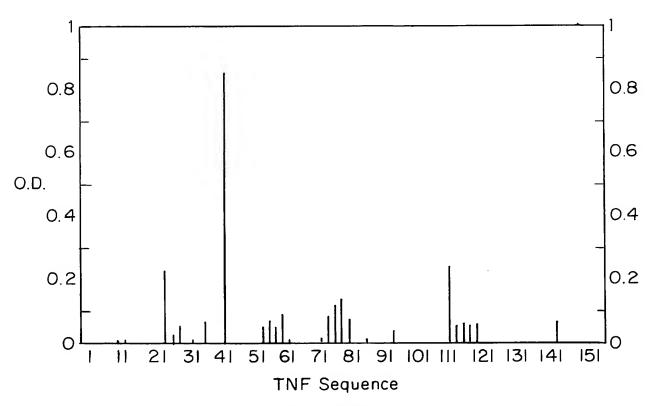


FIG. 14B

				·	 1		
Pro	$\mathtt{Gl}\mathtt{y}$	Ser	Ile	Pro	Leu	Asp	
Asn	Asn	Tyr	${ m Th} r$	Ser	Tyr	Pro	
Ala	Ala	Ile	His	Lys	Ile	Arg	
Val)	Ile	Pro	Asn	Leu
Val	Leu Leu	Tyr Leu	Leu Thr	Ala	Glu	Ile	Ala]
His	Ala 1	Leu G	Leu J	Ser 1	Tyr (Glu :	Ile A
Ala I	Asn A		Val I	Ten 8	Trp	Ala (Ile]
	Ala 1	Glu Gly	His V	Leu J	Pro 3	Ser A	G1y]
Pro Val	Arg 1	Ser (Thr I	Asn I	Lys I	Leu S	Phe (
Lys]	Arg 1	Pro 9	Ser	Val A	Ala J	Arg I	$\mathtt{T}\mathtt{yr}$ 1
10 Asp]	30 Asn <i>i</i>	50 Val 1	70 Pro 9	90 Lys	110 Glu i	130 Asp <i>i</i>	150 Val
Ser	Leu Z	Val	Cys]	Thr]	Ala (Gly A	Gln
Pro :	Trp]	Leu 1	G1y (Gln .	G1y 2	Lys (Gly (
Thr	Gln	Gln]	Gln (Tyr (Glu (Glu]	Ser (
Arg '	Leu (Asn (Gly (Ser	Pro (Leu (Glu :
Ser	Gln .	Asp	Lys (Val	Thr	Gln .	Ala (
Ser	Gly (Arg J		Ala '	Glu '	Phe (Phe
Ser	Glu (ren 1	Leu Phe	Ile ,	Arg (
Arg 9	Ala (Glu Leu Arg Asp	Val 1	Arg :	Gln 1	Gly Val	Leu Asp
1 Val A	21 Gln /	41 Val (61 Gln 1	81 Ser 7	101 Cys (121 Gly (141 Tyr 1

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTGTGAGTCCAGGAGAAAGAGTCCAGT ${\tt AspIleLeuLeuThrGlnSerProAlaIleLeuSerValSerProGlyGluArgValSer}$ TTCTCCTGCAGGCCAGTCAGTTCGTTGGCTCAAGCATCCACTGGTATCAGCAAAGAACA $\tt Phe SerCysArgAlaSerGlnPhe ValGlySerSerIleHisTrpTyrGlnGlnArgThr$

AATGGTTCTCCAAGGCTTCTCATAAAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCC ${\tt AsnGlySerProArgLeuLeuIleLysTyrAlaSerGluSerMetSerGlyIleProSer}$

AGGTTTAGTGGCAGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT ${\tt ArgPheSerGlySerGlyShrAspPheThrLeuSerIleAsnThrValGluSer}$ GAAGATATTGCAGATTATTACTGTCAAGAAAGTCATAGCTGGCCATTCACGTTCGGCTCG GluAspIleAlaAspTyrTyrCysGlnGlnSerHisSerTrpProPheThrPheGlySer

GGGACAAATTTGGAAGTAAAA GlyThrAsnLeuGluValLys FIG. 16A

Docket No. 0975.1005-036 Title: Methods of Treating Neurodegenerative......

Inventors: Junming Le, et al.

GAAGTGAAGCTTGAGGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTC ${\tt GluValLysLeuGluGluSerGlyGlyGlyLeuValGlnProGlyGlySerMetLysLeu}$

SerCysValAlaSerGlyPheIlePheSerAsnHisTrpMetAsnTrpValArgGlnSer TCCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGGGTCCGCCAGTCT

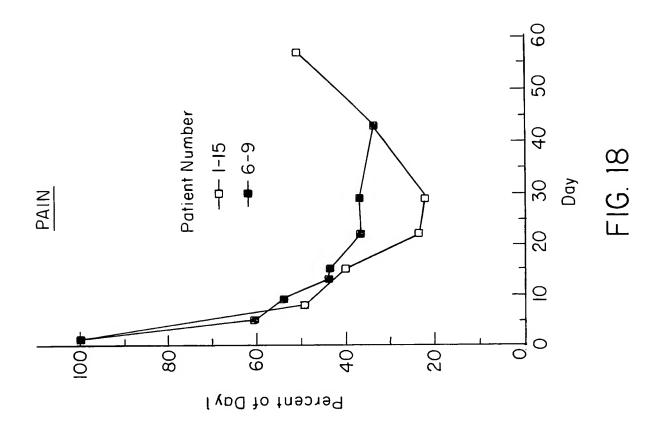
CCAGAGAAGGGGCTTGAGTTGCTGAAATTAGATCAAAATCTATTAATTCTGCAACA $\tt ProGluLysGlyLeuGluTrpValAlaGluIleArgSerLysSerIleAsnSerAlaThr$

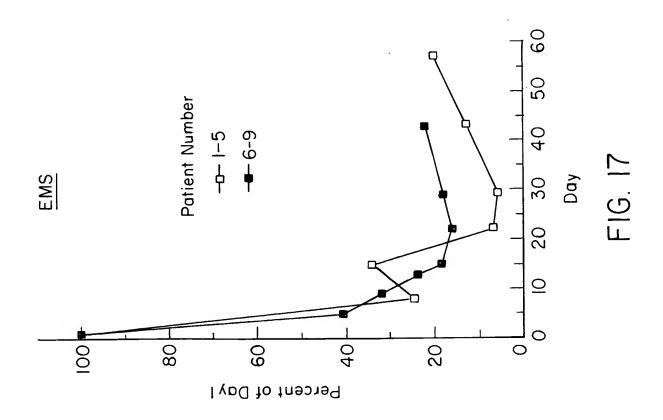
HisTyrAlaGluSerValLysGlyArgPheThrIleSerArgAspAspSerLysSerAla CATTATGCGGAGTCTGTGAAAGGGAGGTTCACCATCTCAAGAGAGATGATTCCAAAAGTGCT

GTGTACCTGCAAATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG $\verb|ValTyrLeuGlnMetThrAspLeuArgThrGluAspThrGlyValTyrTyrCysSerArg| \\$

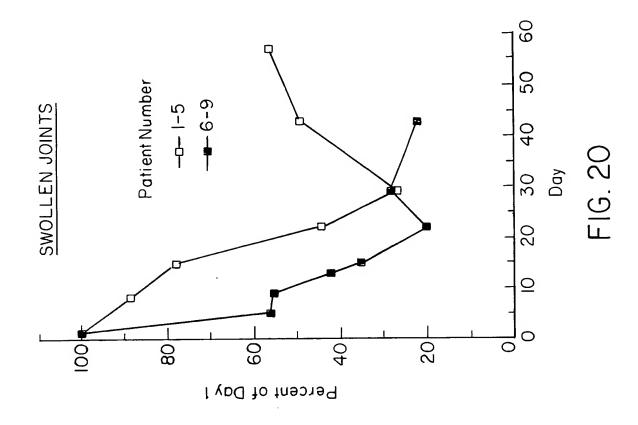
AsnTyrTyrGlySerThrTyrAspTyrTrpGlyGlnGlyThrThrLeuThrValSer AATTACTACGGTAGTACCTACGACTACTGGGGCCAAGGCACCACTCTCACAGTGTCC

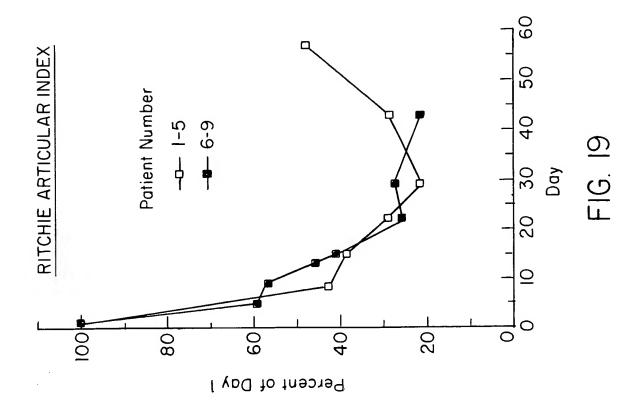
FIG.





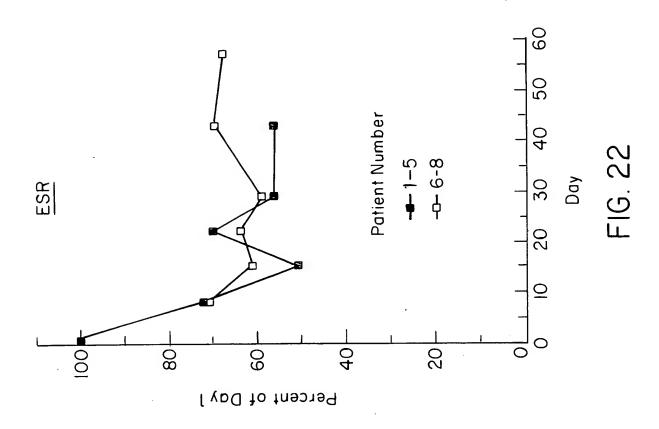
Inventors: Junming Le, et al.

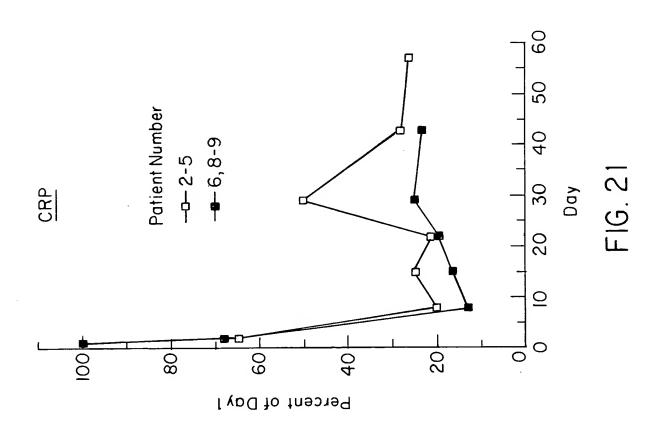




Docket No. 0975.1005-036

Title: Methods of Treating Neurodegenerative.......
Inventors: Junming Le, et al.





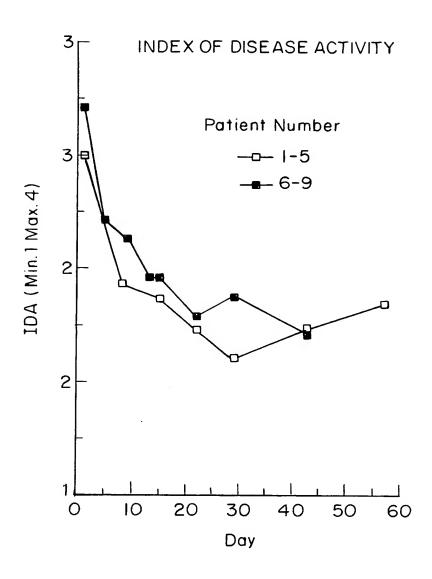
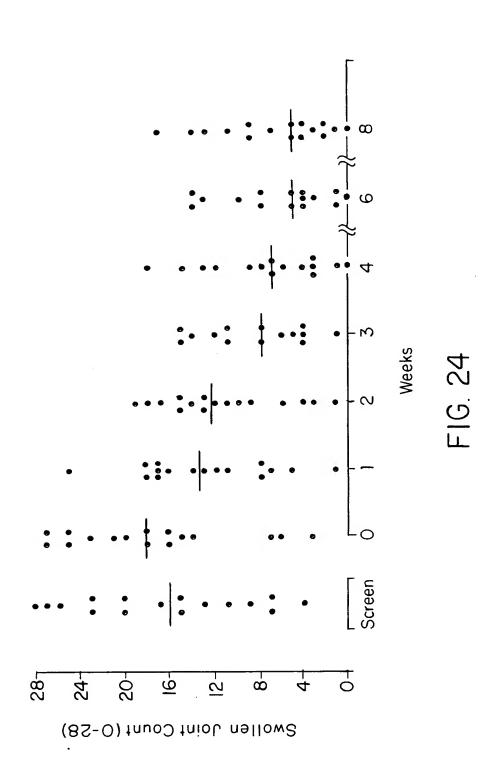


FIG. 23

Docket No. 0975.1005-036

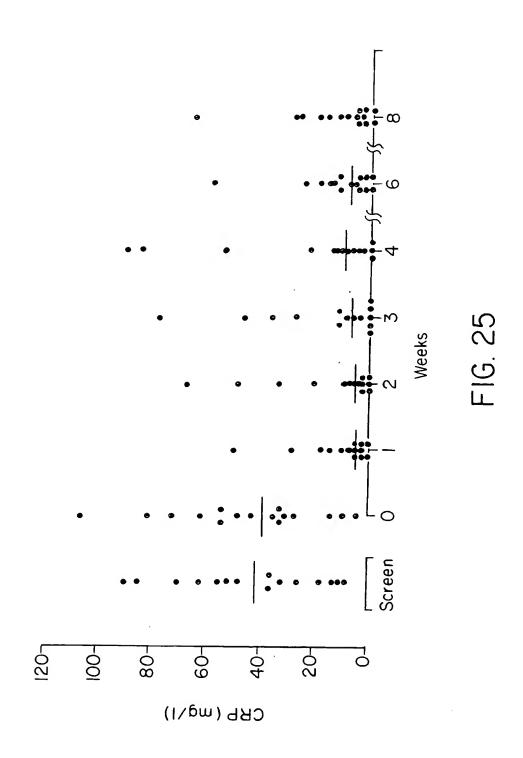
Title: Methods of Treating Neurodegenerative......

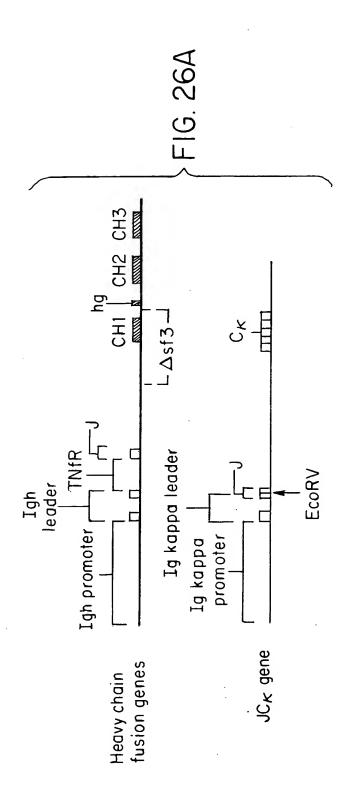
Inventors: Junming Le, et al.

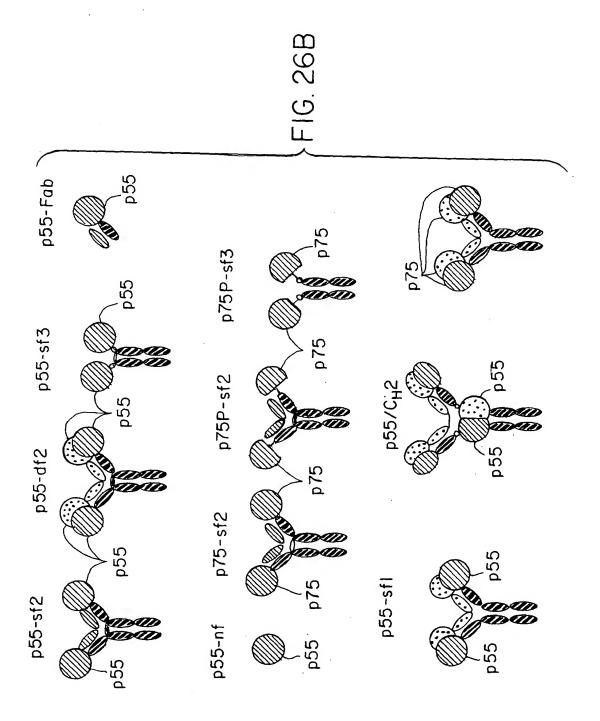


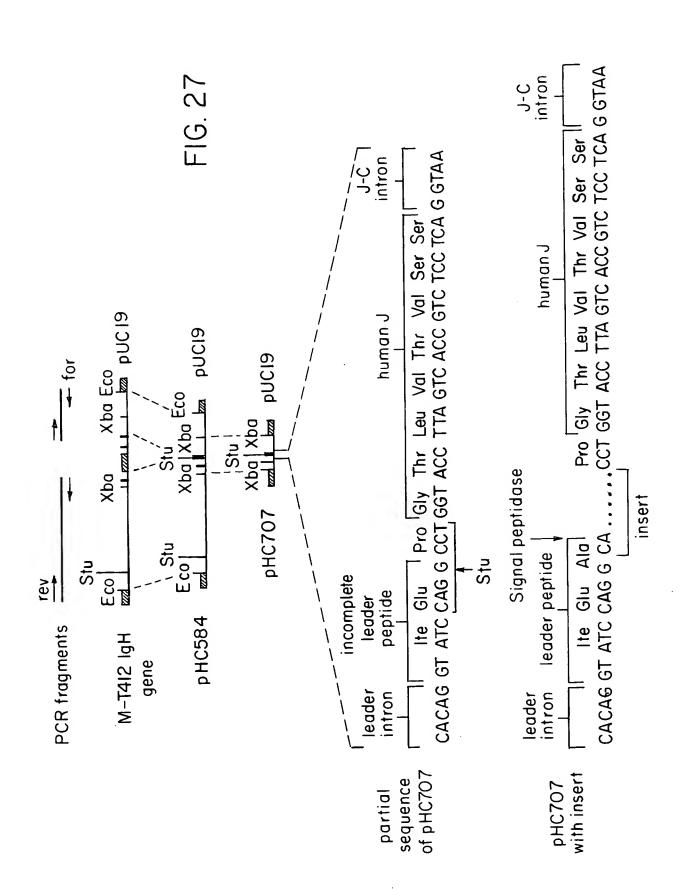
Docket No. 0975.1005-036

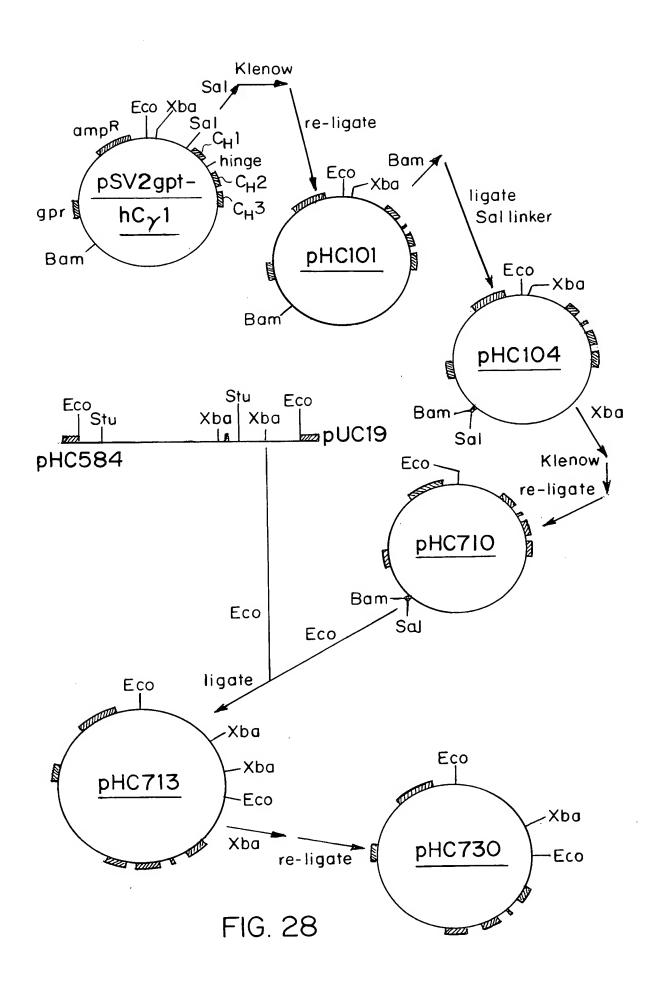
Title: Methods of Treating Neurodegenerative....... Inventors: Junming Le, *et al.*

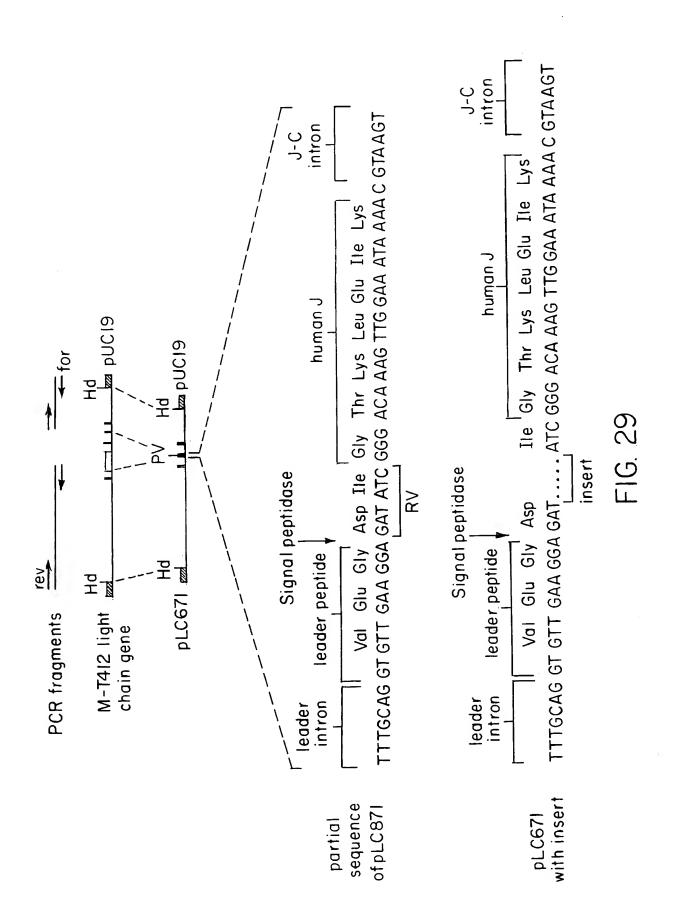












Hd ligate Bam amp^R Sal linker Kpn⁺ ligate Hd pSV2gpt-Kpn-blunt hCĸ PCR-trag. pLC95 Hd Kpn-RV Bam Sal pLC327 Kpn-Bam Hd RVHdSal pLC671 Ήd Hdligate Hd

FIG. 30

Kpn-

 Bam

Sal

pLC690

-RV

-Hd

Docket No. 0975.1005-030 Title: Methods of Treating Neurodegenerative.......

Inventors: Junming Le, et al.

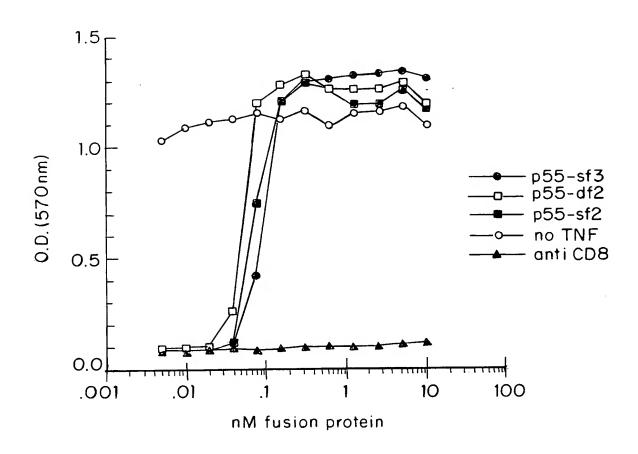


FIG. 31A

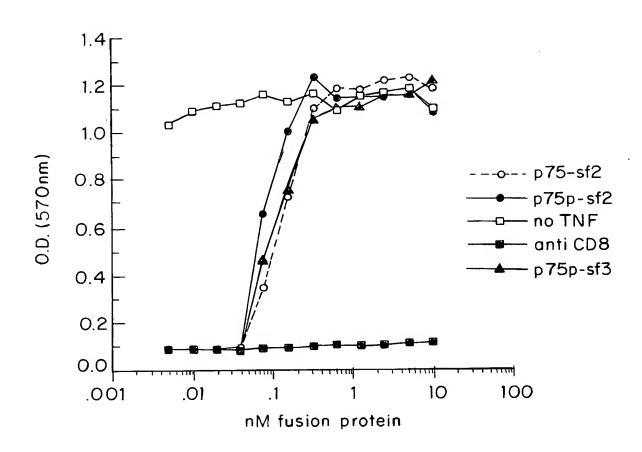


FIG. 31B

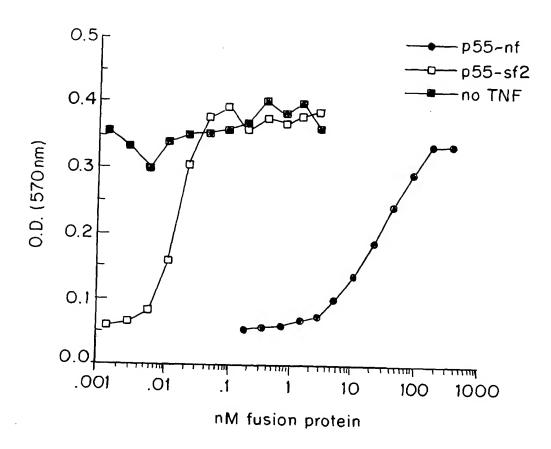


FIG. 31C

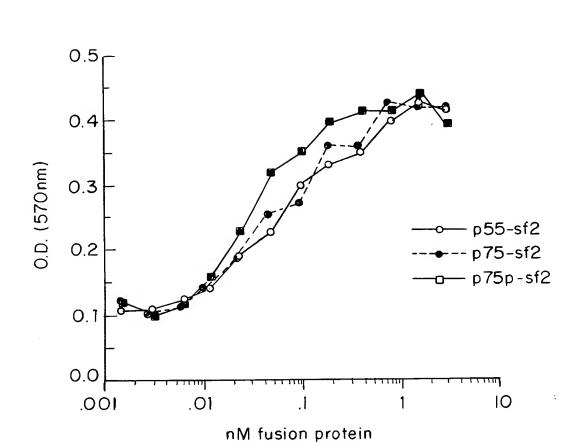


FIG. 32

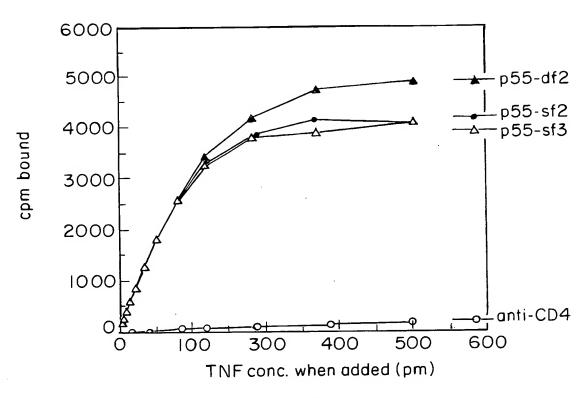


FIG. 33A

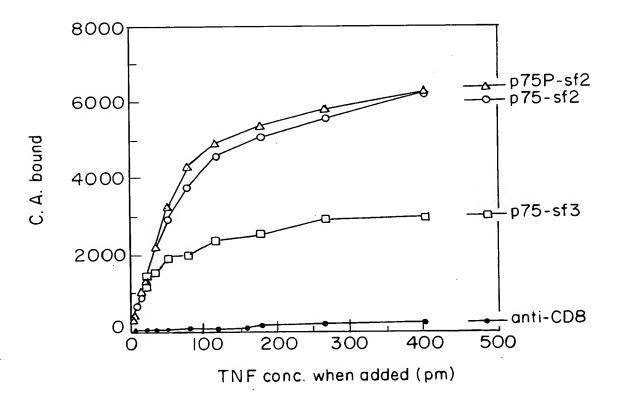
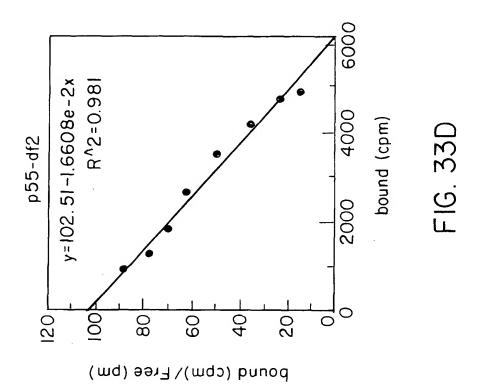
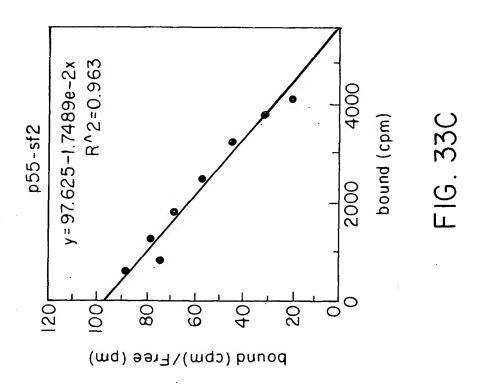
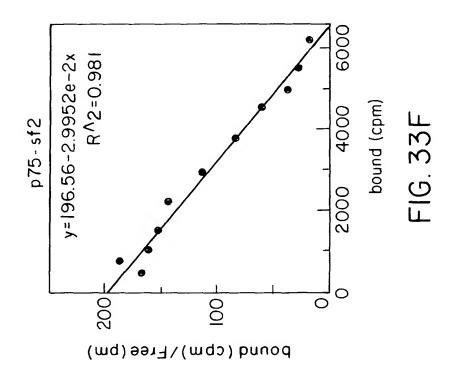
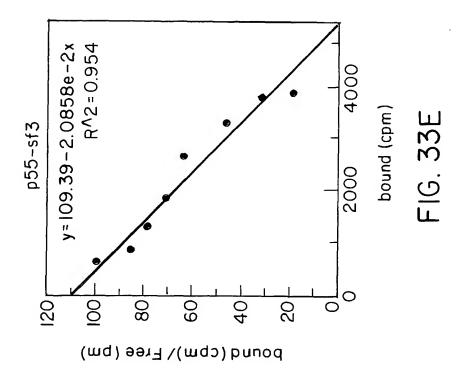


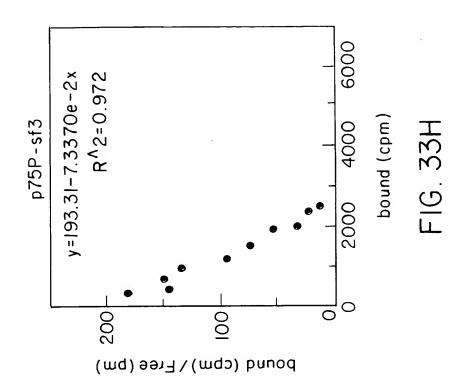
FIG. 33B

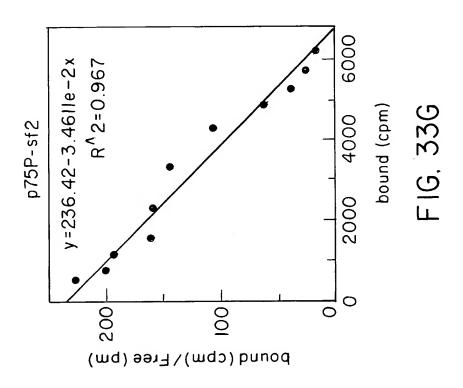


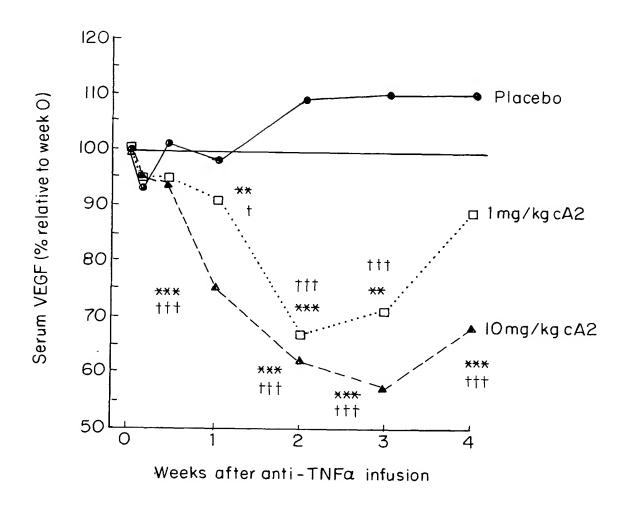












* p \leq 0.05, **p \leq 0.01, *** p \leq 0.001 *versus* pre-infusion † p \leq 0.05, ††p \leq 0.01, ††† p \leq 0.001 *versus* change in placebo group

FIG. 34